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# **REMARKS**

Favorable reconsideration and allowance of the claims of the present application are respectfully requested.

In the present Office Action, Claims 1-9, 12, 13 and 15-23 stand rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. Specifically, the Examiner alleges that the claims contain subject matter that was not described in the specification at the time the application was filed. In particular, the term "macroemulsion" recited in Claims 1, 12 and 17 allegedly lacks support from the originally filed application.

Claims 1-9, 12, 13 and 15-23 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which the applicants regard as their invention.

In response to the § 112 rejections, applicants have amended Claims 1, 12 and 17 by deleting the term "macroemulsion". Applicants submit that the claimed invention is related to a regular emulsion, not a nanoemulsion as is the subject matter of U.S. Patent No. 6,488,702 to Cauwet-Martin. Hence, the claimed invention relates to a regular emulsion which by definition, See Table 1.1 (Macroemulsions vs microemulsions) on Page 5 of the excerpt from "Emulsions: Theory and Practice" Third Edition by Paul Becher<sup>1</sup>, contains droplets in the "Micrometers" range. This is more precisely defined on Page 12 of the article by Jean-Louis Salager, et al., "Nanoemulsions: where are they

<sup>&</sup>lt;sup>1</sup> A copy of the relevant portions of this reference (Ref. 1) is included in Exhibit 1, which is attached with the Response.

going to?", Colloidi, Tpoint 2/2003 pp-12-14.<sup>2</sup>: "...the usual range (1 – 100 micron) for usual macroemulsions". Such a system does not fall under the category of a microemulsion which includes droplets whose diameter is between "0.01 – 0.001 μm" (See Table 1.1 on Page 5 of Ref. 1). Thus, although the specification does not specifically mention that the emulsion is a macroemulsion, one skilled in the art would know that the term "emulsion" and "macroemulsion" are interchangeable used (See also Page 4 of Ref. 1: "... the unadorned word "emulsion" should be understood to mean macroemulsion") and are different from nanoemulsions (See Page 12 of Ref. 2: "...it [the drop size of a nanoemulsion] is usually around 100 nm, and broadly speaking in the 50 – 500 nm range...) which are the subject matter of the Cauwet-Martin reference cited in the present Office Action (See claim 1 (B) in there: ".... oil-in-water emulsion having oil globules with a mean size of less than 150 nm...").

To further show that the term "emulsion" is interchangeably used with the term "macroemulsion", applicants refer to Fig. 1 of Ref. 2. Specifically, Fig. 1 illustrates the differences between micelles, microemulsions, nanoemulsions and (macro)emulsions. Applicants observe that in this reference the terms "emulsion" and "macroemulsion" are also used interchangeably.

In view of the evidence provided in Exhibits 1 and 2, applicants submit that it is well known to those skilled in the art that the term "emulsion" describes a macroemulsion, which is distinct from microemulsions or nanoemulsions. Although the terms "emulsion" and "macroemulsion" are interchangeable in the art, applicants have amended the claims to remove the term "macroemulsion".

<sup>&</sup>lt;sup>2</sup> This reference (Ref. 2) is included in Exhibit 2 attached to this Response.

Based upon the above amendments to Claims 1, 12 and 17, applicants submit that the rejections under § 112, first and second paragraphs, have been obviated.

Reconsideration and withdrawal of the formal grounds of rejection are thus respectfully requested.

Applicants have also amended Claim 2 to include the correct spelling of the term "stabilizer", and have amended Claims 3, 4, 19 and 20 by changing the term "polar" to "hydrophilic". Applicants note that the two terms have the same meaning in the art and thus can be interchangeably used.

Claims 1-9 and 12, 13, and 15-23 stand rejected under 35 U.S.C § 103 as allegedly unpatentable over U.S. Patent No. 6,488,780 to Cauwet-Martin.

With respect to the obviousness rejection citing the disclosure of Cauwet-Martin, applicants submit that the claims of the present application are not obvious from Cauwet-Martin for the following reasons: Cauwet-Martin provides detergent and conditioning compositions having a washing base composed of surface active agents with a detergent powder and a conditioning system which is in the form of a nanoemulsion. In particular, the conditioning system is described at Col. 1, lines 54-56 as comprising at least one oil-in-water emulsion having oil globules with a mean particle size of less than 150 nm.

Nanoemulsions are clearly differentiated from the emulsion, i.e., macroemulsion, appearing in the example at Col. 12, line 65-Col. 14, line 12.

In the example, the comparative composition, i.e., composition B, is a macroemulsion (i.e., a regular emulsion) which has oil globules of approximately 1500 nm. See Col. 15, lines 57-58. This example outlines that the use of nanoemulsions is *critical* for the stability of the detergent and conditioning composition. In particular, at

Col. 13, lines 62-64, it is stated that "[T]he composition B is unstable and the oil separates out at the surface of the liquid, whereas the composition A is homogeneous and stable." Thus, Cauwet-Martin clearly teaches and suggests that stable compositions are only obtained in instances in which the emulsion is in the form of a nanoemulsion, irrespective of the type of emulsifier being used.

The nanoemulsion of the prior art reference described in the example contains two organic emulsifiers (nonionic and ionic), avocado oil, ethanol, glycerin and water, and it is reported to have oil globules of approximately 60 nm. From the disclosure of Cauwet-Martin, it is obvious that the way in which the emulsion is prepared (i.e., nanoemulsion vs. macroemulsion) is decisive for the achievement of a stable composition. Cauwet-Martin discloses that polyether siloxanes are preferred non-ionic amphiphilic lipids (see, Col. 5, lines 25-50), i.e., emulsifiers for the production of nanoemulsions, but not mandatory as can be seen in the given example. For the production of nanoemulsions, the prior art reference requires that a high-pressure homogenizer be used. See Col. 13, lines 36-37.

In contrast to the disclosure of Cauwet-Martin, the present invention provides emulsions prepared using a conventional procedure (see, for example, the preparation procedure mentioned in Example 8). Hence, applicants' claimed invention is directed to regular emulsions, not nanoemulsions. As indicated above, applicants' use of the term "emulsion" represents to one skilled in the art that the present invention is directed to macroemulsions, as is evident by the two articles contained in Exhibits 1 and 2. The unexpected finding of the present invention, which is described at Page 5, line 26-Page 6, line 20, may be summarizes as follows: Only by using a selected and specific type of

polyether siloxane of formula I in combination with stabilizers known from the state of the art can one obtain homogeneous and stable (silicone oil-free) oil-in-water (macro)emulsions.

According to the teaching of Cauwet-Martin, on the other hand, (macro)emulsions using polyether siloxanes or any other type of emulsifier would be unstable. Hence, the disclosure of Cauwet-Martin teaches away from the claimed invention in which stable emulsions containing a specific polyether siloxane emulsifier can be obtained without the need of forming nanoemulsions.

Moreover, one skilled in the art expects that the addition of stabilizers would lead to stable emulsions. It is, however, experienced that the addition of stabilizers is not sufficient to obtain homogeneous and stable (silicone oil-free) oil-in-water emulsions by using polyether siloxanes known in the art. See Example 9 of the present application. The teaching of the present application is that only a selected and specific type of polyether siloxane of formula I is compatible with commonly used stabilizers and that the claimed polyether siloxanes can be used to form homogeneous and stable emulsions (see Examples 8 and 9). The claimed polyether siloxanes are characterized as relatively hydrophobic amphiphiles, whereas classical oil-in-water emulsifiers are characterized as strongly hydrophilic ones.

The § 103 rejection also fails because there is no motivation in the applied reference which suggests modifying the disclosed compositions to include a regular emulsion, instead of a nanoemulsion. Thus, there is no motivation provided in the applied references, or otherwise of record, to make the modification mentioned above. "The mere fact that the prior art may be modified in the manner suggested by the

Examiner does not make the modification obvious unless the prior art suggested the desirability of the modification." <u>In re Vaeck</u>, 947 F.2d, 488, 493, 20 USPQ 2d. 1438, 1442 (Fed.Cir. 1991).

It is again emphasized that Cauwet-Martin teaches away from the claimed invention since in the prior art disclosure an example is provided in which the use of a macroemulsion (i.e., a regular emulsion) which had oil globules of approximately 1500 nm did not work in stabilizing a detergent or conditioning composition. This comparative example provided in Cauwet-Martin indicates that the use of nanoemulsions is *critical* for the stability of the detergent and conditioning composition. Cauwet-Martin thus clearly teaches and suggests that stable compositions are only obtained in instances in which the emulsion is in the form of a nanoemulsion, irrespective of the type of emulsifier being used. Thus, the applied reference teaches away from using macroemulsions of the type presently claimed. Applicants submit that the applied reference should be considered as a whole, and portions arguing against or teaching away from the claimed invention must be considered. See, for example, <u>Bausch & Lomb, Inc</u> v. Barnes-Hind/Hydrocurve, Inc., 7967 F.2d, 443, 230 USPQ 416 (Fed.Cir. 1986). Applicants further opine that a reference is relevant for all it teaches to those skilled in that art. See, for example, In re Fritch, 972 F.2d 1260, 23 USPQ 2d 1780 (Fed. Cir. 1992). Thus, since Cauwet-Martin discloses that macroemulsions can not be used to stabilize detergents and conditioning compositions, one skilled in the art would not consider to use such emulsions in cosmetic or pharmaceutical preparations.

In view of the above remarks, the rejection under 35 U.S.C. § 103 has been obviated. Applicants therefore request reconsideration and withdrawal of the instant §103 rejection.

Thus, in view of the foregoing amendments and remarks, it is firmly believed that the present case is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,

Leslie S. Szjvos, Ph.D. Registration No. 39,394

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Enclosures Exhibits 1 and 2

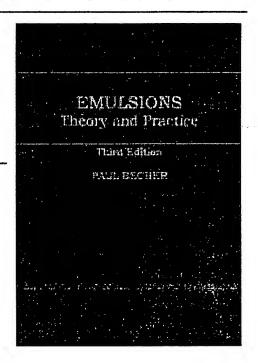
 
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# Emulsification Reference from C.H.I.P.S.

# **Emulsions:** Theory and Practice

# Third Edition by Paul Becher

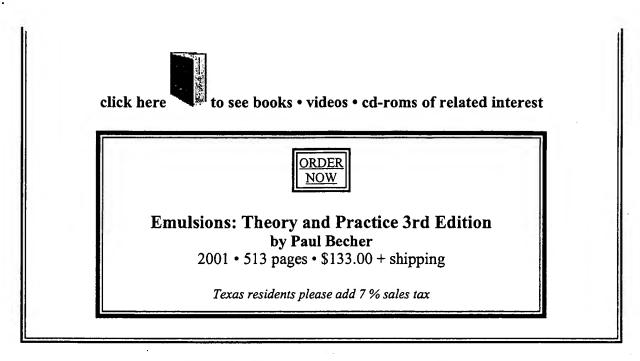
Emulsions: Theory and Practic is an introduction to the study and formulation of emulsions. It discusses background theory, the physical properties of emulsions, theories of emulsion stability and instability, emulsifying agents and their chemistry, formulation procedures and techniques, and industrial applications of emulsification and demulsification.



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# Introduction and Definitions

Oil and water don't mix.

—Old Proverb

It is impossible to overestimate the importance of emulsions, both from the view-point of basic theory and of their multifarious applications. The theoretical basis underlying emulsions comprises the greater part of the background to colloid and surface science, and, in some instances, a substantial contribution from other branches of science, with some special emphasis on the biological.

With respect to the applications of emulsions, one may distinguish between naturally occurring systems and man-made ones. Examples of naturally occurring emulsions are those connected with mammalian physiological processes, for example, lactation, digestion of food, and so on. As for man-made applications, the number of areas in which emulsions are used is great, including, in a far from inclusive list, foods, paints, cosmetics, pharmaceuticals, explosives, rocket fuel, and so on.

One may, as well, construct a long list of *undesirable* emulsions, such as oil-field emulsions, and so on.

The first mention of what is undoubtedly a man-made emulsion dates to the second century, when the Greek physician, Galen, described a sort of cold cream (1). The word itself did not enter the language until the 17th century, and owes its derivation from the Latin *mulgere*, to milk, descriptive of the milky appearance of many macroemulsions.

The first two editions of this book (2, 3), especially the second edition, still may serve as useful references. In addition, deeper discussion of many of the topics covered in the present volume will be found in the four volumes of the *Encyclopedia of Emulsion Technology* (4). In this chapter, we will define many of the important terms which will be used in the present volume. Additional definitions will be introduced as appropriate.

#### **DEFINITIONS**

It is useful to begin by making the distinction between macroemulsions and microemulsions, a distinction which was unnecessary in earlier discussions. Although the existence of microemulsions was noted in the earlier editions, the vast amount of theory and data concerning microemulsions which has been accumulated over the past quarter-century (mostly in connection with enhanced oil recovery) makes the distinction an important one.

#### Macroemulsions

Earlier, a number of definitions of the word "emulsion" culled from the literature were presented, mostly to expose their deficiencies. Herewith is reproduced only the author's definition from earlier editions, perhaps to expose *its* deficiencies:

An emulsion is a heterogeneous system, consisting of at least one immiscible liquid intimately dispersed in another in the form of droplets, whose diameters, in general, exceed 0.1  $\mu$ m. Such systems possess a minimal stability, which may be accentuated by additives such as surface-active agents, finely divided solids, etc.

The most striking deficiency is in the definition of smallest particle size; the limitation imposed has no theoretical basis, but is merely an indication of the limits of measurement at the time the definition was written. It is, for all practical purposes, slightly smaller than the smallest particle that can be observed with an optical microscope or measured with a sizing device, such as the *Coulter Counter*.

The development of more sophisticated particle-sizing techniques, such as photon correlation spectroscopy (PCS), have demonstrated that emulsions may contain droplets much smaller than this, well into the nanometer range, and indeed overlapping the size range of microemulsions (see below and Chapter 9). Consequently, it appears that this lower size range could properly be removed from the above definition, which could otherwise be allowed to stand.

Recently, emulsions containing these very small droplets have been given the name *miniemulsions*. There seems to be no real need for this designation, because it implies a (nonexistent) distinction between these systems and emulsions consisting of larger droplets.

However, in order to distinguish between the emulsion system defined above, and the so-called microemulsions, the designation *macroemulsion* is useful; miniemulsions thus become "macroemulsions containing very small droplets."

In the remainder of this book, however, the unadorned word "emulsion" should be understood to mean macroemulsion.

One other qualification is necessary. The phases making up an emulsion must, by definition, be liquids at the time the emulsion is formed. However, if one or both of the phases are solids at normal (i.e., room ambient) temperatures, it may be necessary to produce the emulsion at an elevated temperature; then, at ambient temperatures one or the other (or both) phases could be solid. An example of this would be the old-fashioned type of floor wax formulation, in which the internal wax phase is a solid at room temperature. Similarly, some polymer latices are produced in this manner (e.g., those of polyethylene). More recently, emulsions (e.g., emulsion explosives) have been developed in which the external phase, and

sometimes the internal phase, are solid under use conditions. Although these are in appearance far from our classical conception of an emulsion, they are often designated emulsions, in spite of the fact that this author had argued earlier that such systems could not properly be considered true emulsions. Such systems might be more properly described as *suspensions*, but in practical usage they are often still described as emulsions. This usage may be of considerable importance in connection with patents and patent litigation.

Recently, it has been observed that it is possible to have an emulsion in which only a portion of the droplets have solidified (5,6). Such systems may further solidify in a time-dependent manner; presumably the progressive solidification occurs as a result of collisions between liquid and solid drops, in which the solid drop may be thought of as "seeding" the other. The rate at which this occurs is apparently dependent on the nature of the emulsifying agent (7).

#### Microemulsions

The term "microemulsion" was invented by Schulman and Montagne (8) to describe the transparent emulsions reported earlier by Schulman and Bowcott (9). It was, perhaps, an unfortunate choice of nomenclature, because microemulsions, strictly speaking, are not emulsions at all. On the other hand, because they consist of a dispersion of immiscible liquids (an oil phase and an aqueous phase), stabilized by surface-active agents, the choice of the word appears inevitable.

Some of the similarities and differences between macro- and microemulsions are presented in Table 1.1. The important distinction between microemulsions and macroemulsions corresponds to the last two entries in the table; namely, the fact that the former are, in general, considered to be thermodynamically stable, whereas the latter are not. This distinction is sometimes of practical importance (although this may be overstated), as conferring infinite stability on microemulsions. This, obviously, cannot be experimentally verified.\* It should, in fact, be observed that the infinite stability of microemulsions may have environmental (that is, storage) limitations (10). A microemulsion may be defined as follows:

Table 1 1	Moore	emulsions	mieroe	mulaiona
Table 1.	i Macro	nemilisions	vs microe	muisions

Property	Macro	Micro
Components	Oil-water-surfactant	Oil-water-surfactant
Surfactant number	One or more	One or more (usually at least two)
Surfactant types	All	All
Surfactant concentration	Fairly low	Fairly high
Droplet size	Micrometers	0.01-0.001 μm
Thermodynamic stability	Unstable	Stable
Storage stability	Formulation-dependent	Infinite (?)

<sup>\*</sup>The problem is that such a measurement takes a very long time!

#### 6 Emulsions: Theory and Practice

A microemulsion is a heterogeneous system, consisting of at least one immiscible liquid dispersed in another. The droplet size in a microemulsion is usually smaller than the wavelength of visible light, and, consequently, microemulsions are transparent or, at least, translucent. They are stabilized by the use of a mixture of surface-active agents, one of which is a short-chain-length amphiphile, possessing limited water solubility (e.g., pentanol). Microemulsions are characterized by the existence of ultralow interfacial tensions (of the order of less than  $10^{-2}$  mN/m), and, frequently, by the presence of liquid-crystalline forms of the mixture of surface-active agents at the oil-water interface.

Microemulsions will be further discussed in Chapter 9.

More complete definitions in the area of colloid and surface science generally are to be found in the dictionaries compiled by Becher (11) and Schramm (12).

### UNITS

In the earlier editions of this book, CGS units were used almost exclusively. However, in the more recent literature, SI (Système Internationale) units have been coming more frequently into use (or, in many cases, a mixture of CGS and SI). Ramaswamy and Rao (13) give a useful discussion of SI units. In references to the literature, the units employed by the original author will usually be retained.

## TERMINOLOGY OF EMULSIONS

The basic terminology of emulsions (and, for that matter, of all dispersions) owes its origin to Wa. Ostwald (14), who pointed out that eight types of dispersions of two mutually insoluble substances could exist:

- 1. Liquid-in-liquid
- 2. Solid-in-liquid
- 3. Gas-in-liquid
- 4. Liquid-in-solid
- 5. Solid-in-solid
- 6. Gas-in-solid
- 7. Liquid-in-gas
- 8. Solid-in-gas
- 9. Gas-in-gas

The ninth possibility, that is, gas-in-gas, was ruled out by Ostwald, on the grounds that all gases are mutually and completely soluble in one another. There are some reasons to think that there may be exceptions to this, but they need not concern us here.

It is convenient to abbreviate these classes of dispersions by referring to them as L/L, S/L, G/L, L/S, S/S, G/S, L/G, S/G, and (if it indeed does exist) G/G, respectively. Obviously, it is the first class of dispersions (liquid-in-liquid) that is of principal concern in this discussion. However, it should be pointed out that S/L (solid dispersions), G/L (foams), S/G and S/L (aerosols, smoke, fog) are largely governed

by the same theoretical considerations which apply to L/L systems, that is, emulsions.

Referring to a point made earlier (in connection with the definition of emulsion, above), it is apparent that the final state of an emulsion may well be almost indistinguishable from an S/L or S/S dispersion. Our guidance here would be the information about the production of the emulsion; thus, if under the conditions of manufacture the system could be described as L/L, the fact that a later change in experimental conditions (e.g., reduction of temperature, polymerization, etc.) rendered one or both of the phases solid should not require retitling the system under study. Although this distinction may seem almost trivial, it could be important in the area of patents.

In fact, the use of the word "suspension," as used previously is usually understood to refer to *solid-in-liquid* systems; however, it should be pointed out that, broadly, any one of the classes defined by Ostwald may be so designated. This could result in confusion; however, the type of suspension is frequently obvious from the context.

## Components

Because traditionally the components of an emulsion have been water and oil, it has become the custom to refer to both macro- and microemulsions as being water-in-oil (W/O or w/o) or oil-in-water (O/W or o/w). This usage continues, even though it is understood that the water phase may in fact contain dissolved electrolyte, lower alcohols, and so on, or indeed not be water at all, but rather some polar liquid (e.g., various glycols). At the same time, the oil phase may not precisely meet the definition of an oil, but be *any* liquid insoluble in water (e.g., silicones, fluorocarbons, nitroglycerine, etc.).

The useful term *morphology* to describe the status of the components of an emulsion, for example, by D. Smith (15), has been introduced.

It is also customary to refer to the dispersing liquid as the *continuous* or *external* phase, while the dispersed liquid is referred to as the *discontinuous* or *internal* phase. The concentration of the internal phase is usually expressed in volume terms; either as the volume fraction or as volume per cent. It is also customary to use the symbol  $\phi$  (or  $\varphi$ ) to represent the phase volume concentration (in either units).

Another method to describe the composition of the emulsion is the term water/oil ratio (abbreviated WOR), introduced in certain discussions of enhanced oil recovery. The term defines itself, but there is a certain ambiguity in the term; it is not always clear whether the WOR is expressed in weight or volume terms, nor does it define the morphology of the emulsion (o/w or w/o). When these two parameters are defined, on the other hand, the relation between WOR and  $\phi$  is a simple arithmetic one.

In addition, the concentration of the third component of the emulsion, that is, the surface-active agent, may be expressed in a number of ways. It may, for example, be given in terms of its concentration in the total emulsion, or as a percentage of the amount of internal phase. In certain situations, one or the other method may be appropriate. For example, in a manufacturing formulation, concentration as a percentage of the total would be most convenient, whereas in a case where one wished to emphasize the relation between the internal phase concentration and the quantity of emulsifying agent, the second method would be better. Obviously, the two methods

# Nanoemulsions: where are they going to?

Jean-Louis Salager, Laura Marquez, Ana Forgiarini/Lab. FIRP, University of the Andes – Mérida (Venezuela) Lucilla Del Gaudio/EniTecnologie

In questi ultimi anni sta emergendo una nuova tecnologia che investe trasversalmente numerosi settori industriali con enormi potenzialità: la tecnologia delle nanoemulsioni ovvero di emulsioni in cui la fase dispersa ha dimensioni tra i 50 e 100 nanometri.

I relativi metodi di preparazione finora impiegati utilizzano mixer ad alta energia e quindi alti costi e impossibilità di impiego in settori industriali a minor valore aggiunto, quali l'upstream e il downstream.

Attualmente alcuni prestigiosi centri di ricerca, hanno evidenziato l'esistenza di nuove strade "a bassa energia" per formulare nanoemulsioni.

Tali recenti sviluppi rendono interessanti questi sistemi anche nel settore petrolifero, dove molteplici possono essere le loro applicazioni ovunque vi sia la necessità di veicolare componenti insolubili all'interno del mezzo disperdente e/o in sistemi a bassa porosità: drilling fluids, oil, fuels, ecc.

Questo articolo vuole chiarire cosa sono le nanoemulsioni in rapporto alle micro e macroemulsioni (rispetto alle quali si osserva una certa confusione in letteratura), e illustrare gli emergenti approcci detti "gentle methods" per la loro formulazione.

Nanoemulsions can be defined as extremely small droplet emulsions, so small that the interaction of matter with light is very weak and they appear to be transparent or translucent with a bluish coloration. Nanoemulsion is actually a misnomer because the drop size is far larger than a nanometer, e.g., it is usually around 100 nm, and broadly speaking in the 50-500 nm range, e.g. much smaller than the usual range (1-100 micron) for usual macroemulsions. Since an emulsifier molecule size is typically 2 nanometer long, a micelle, i.e., a surfactant molecule aggregate in water is 5 nm or more in diameter. When oil phase molecules enter the micellar core, the aggregate get swollen, sometimes to a large extend, to produce a spherical object whose size can reach 100 nm or more (see figure 1). This could result on a nanoemulsion or not depending of some factors, particularly the physicochemical formulation and the amount of surfactant. In presence of a large amount of surfactant the swollen micelles are very numerous and touch one another, and a bicontinuous microemulsion structure could be achieved at the proper formulation. Microemulsions are really single phase systems in which the structure contains fusioned oil balls and fusioned water balls, with no actually dispersed phase. Microemulsions are flexible near-zero curvature structures whose thermodynamic stability implies an ultra low interfacial tension so that interfacial deformation is easy. In other words a microemulsion is not an emulsion with small droplets, but some kind of weaved complex fabric with oil and water interconnected domains. Emulsion with small droplets in the 50-1.000 nm range should be called miniemulsion, but the term nanoemulsion has prevailed, probably because it implies an even smaller drop size and it has become more suitable for

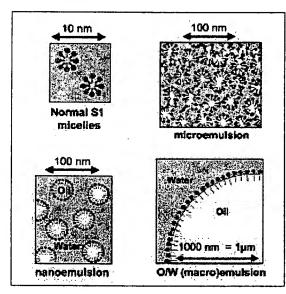


Figure 1: different oil/water structures

commercial issues. The point is that the mini- or the so called nano-emulsions are true emulsions with dispersed phase droplets and a continuous phase, and a surface area which is much smaller than a microemulsion, thus requiring much less surfactant.

# How can we make nanoemulsions?

Nancemulsions are persistent only if the formulation is far away from the so-called "optimum formulation" in which the surfactant exhibits an equal affinity for both the oil and water phases, and for which a low tension is attained. Hence, nancemulsion stability implies a high interfacial tension, and thus a considerable surface energy (which is the tension times the surface area). As a consequence, it is extremely difficult to make nancemulsions by brute force stirring, and if done so, it requires an extremely large amount of energy. Recent investigations have shown that some formulation-stirring conditions can be much more efficient than others to produce fine emulsions, but they still demand a huge amount of energy.

From what has been discussed above, it is evident that the size of the structural oil or water domains in a microemulsion can be essentially similar to the droplet size in a nanoemulsion. Passing from a microemulsion to a nanoemulsion could be thus an almost energy-free process, if an appropriate change is found. There are actually at least two ways, both called phase transition methods. The first one consists in changing the formulation in such a way that the microemulsion fusioned ball structure breaks up into droplets when the tension increases as a consequence of a change in formulation. This is essentially the so-called "Taylor instability" in which an elongated liquid jet ruptures into droplets, as in modern ink-jet printers. Because of the high coalescence rate inherent to the formulation conditions during the transition, these methods are tricky because the droplets are likely to combine quickly to form large drops, unless something prevents it, as in the famous Phase Inversion Temperature (PIT) method in which a liquid crystal layer encapsulates the droplets. The second class of methods uses a phenomenon which is called "catastrophic inversion", in which an emulsion containing drops of water in oil, suddenly becomes a dispersion of oil in water, or reciprocately. Recent investigations have shown that in some cases this swapping can take place through an intermediate structure so-called multiple emulsion in which the continuous phase is able to deform and create tiny droplet inclusions inside the drops. When the multiple emulsion finally breaks, it can release these extremely fine droplets. Although this method is still under intensive scrutinizing because it involves complex mechanisms that can be interpreted only with discontinuous mathematics such as catastrophe theory, it has been used for years to make alkyl resin paints or epoxy coatings because it requires a small amount of low shear energy, which can be readily provided by an appropriate slow motion gear to mix a 20 ton paint vessel. Very recent investigations, particularly at the FIRP ("Fenomeno, Interfase, Reologia, Proceso") laboratory in Venezuela, has cleared a lot of uncertainties and has shown that the three classes of

methods (brute force stirring, transitional and catastrophic

phase inversions) can be harnessed and combined to

optimize the emulsification process at a low energy cost.

# Nanoemulsion stability

Nanoemulsion droplets are so tiny that gravity has no effect on them. Consequently they would not settle, unless the drop size increases by coalescence through Brownian encounters or another process so-called "Ostwald ripening" which is driven by the Laplace pressure gradient existing between drops of different sizes. Such decaying mechanisms can be inhibited by using a proper surfactant formulation and by making the emulsion as monodispersed as possible. However, score of variables are generally involved in different competitive factors and the attainment of a proper formulation is often a very time-consuming ordeal, unless the research team has a great deal of experience and a deep insight of the physical chemistry phenomena.

# Nanoemulsion applications

Nanoemulsions are currently used in "chic" science utilization such as personal care cosmetics and fancy

health-care vehicles such as parenteral feeding. where their small drop size allows the penetration through the skin, blood capillary or membrane barriers. The current belief that there are expensive to make, and are thus not amenable to more "dirty" or industrial applications, is certainly a consequence of a lack of wide-spread know-how about it, as can be easily deduced from their actual application in the large scale manufacturing of alkyd paints or silicon oil emulsions, in which the know-how is sharp though not optimized. As far as potential applications are concerned in the petroleum industry, at least three of them seem evident, e.g. the dispersion of water droplets in different kinds of fuel in order to curtail exhaust pollution by CO or NOx, the manufacturing of cutting or laminating emulsions for metal working, and the formulation of oil based drilling fluids in which a small amount of tiny water droplets can impart a high viscosity. Beyond these current possibilities, there is a cutting edge evidence that nanoemulsions may be used to stabilize complex last fashion stuffs such as foamy drilling fluids.

## Nanoemulsioni in cattedra

Quindici ricercatori appartenenti a diversi gruppi di ricerca di EniTecnologie ed Eni Divisione E&P hanno partecipato al corso "Nanoemulsion and Science Emulsion" tenutosi presso la sede di Eni Corporate University a San Donato Milanese dal 10 al 13 marzo scorso. I docenti provenivano dal laboratorio di Ricerca FIRP (Università di Mérida in Venezuela) di cui il Prof. Salager è il fondatore e l'attuale direttore. Con tale evento, EniTecnologie ed Eni Corporate University hanno iniziato una stretta collaborazione per lo sviluppo e la promozione delle conoscenze tecnologiche ad alto impatto nel settore petrolifero; in particolare, in questi ultimi anni, il tema delle nanoemulsioni ha guadagnato un enorme interesse scientifico e si prevedono interessanti applicazioni nel settore upstream e downstream. Nonostante gli sforzi di numerosi ricercatori appartenenti ai diversi settori di applicazione (per esempio in campo medico, farmaceutico, cosmetico e per la sintesi di nuovi materiali) non si è ancora giunti a un'esatta comprensione di questo misterioso mondo; del resto non esistono testi specifici sull'argomento e frammentaria risulta la letteratura in merito. È in questo contesto che si è proposto il corso, il cui obiettivo è stato quello di dare un panorama nel campo della formulazione delle emulsioni (ancora troppo spesso trattato in modo empirico e non razionalizzato) con particolare riferimento alle nanoemulsioni.

## Jean-Louis Salager's profile

Prof. Jean-Louis Salager holds a Bachelor of Science in Chemistry and in Process Engineering from University of Nancy (France), and a Master of Science and a PhD in Chemical Engineering from University of Texas at Austin (USA). He is the founder the School of Chemical Engineering and Laboratory FIRP at University of the Andes (Wérida-Venezuela), where is currently an Emeritus Professor in the Chemical Engineering Faculty. His research interests are in physico-chemical formulation with surfactants and properties of emulsions and foams, with applications in petroleum production and other industrial processes. He was granted the Venezuelan National Award for Technological Research and the Simon Bolivar Award. He is a member of the Latin America Academy of Sciences and Regional Editor of Journal of Dispersion Science and Technology (Dekker, New York).